

Israeli R.S., Powell C.T., Fair W.R., Heston W.D.W.;
 RT "Molecular cloning of a complementary DNA encoding a prostate-specific
 membrane antigen.";
 RL Cancer Res. 53:227-230(1993).
 RN [2]
 RP NUCLEOTIDE SEQUENCE [MRNA] (ISOFORM PSMA').
 RC TISSUE-Prostate;
 RX MEDLINE-95188188; PubMed-7882349;
 RA Su S.L., Huang I.-P., Fair W.R., Powell C.T., Heston W.D.W.;
 RT "Alternatively spliced variants of prostate-specific membrane antigen
 RT RNA: ratio of expression as a potential measurement of progression.";
 RL Cancer Res. 55:1441-1443(1995).
 RN [3]
 RP NUCLEOTIDE SEQUENCE [MRNA] (ISOFORMS PSMA-1 AND PSMA-2).
 RC TISSUE-Prostate;
 RX MEDLINE-98041905; PubMed-9375657;
 RA Brzdega T., Turi T., Wroblewska B., She D., Chung H.S., Kim H.,
 Neale J.H.;
 RT "Molecular cloning of a peptidase against N-acetylasparylglutamate
 RT from a rat hippocampal cDNA library.";
 RL J. Neurochem. 69:2270-2277(1997).
 RN [4]
 RP NUCLEOTIDE SEQUENCE [GENOMIC DNA] (ISOFORM PSMA-1), AND VARIANT
 RP HIS-75.
 RX MEDLINE-99057588; PubMed-9838072; DOI=10.1016/S0167-4781(98)00200-0;
 RA O'Keefe D.S., Su S.L., Bacich D.J., Horiguchi Y., Luo Y., Powell C.T.,
 Zandvliet D., Russell P.J., Molloy P.L., Nowak N.J., Shows T.B.,
 Mullins C., Vonder Haar R.A., Fair W.R., Heston W.D.W.;
 RT "Mapping, genomic organization and promoter analysis of the human
 RT prostate-specific membrane antigen gene.";
 RL Biochim. Biophys. Acta 1443:113-127(1998).
 RN [5]
 RP NUCLEOTIDE SEQUENCE [MRNA] (ISOFORM PSMA-1).
 RC TISSUE-Brain;
 RX MEDLINE-98362085; PubMed-9694964;
 RA Luthi-Carter R., Barczak A.K., Speno H., Coyle J.T.;
 RT "Molecular characterization of human brain N-acetylated alpha-linked
 RT acidic dipeptidase (NAALADase).";
 RL J. Pharmacol. Exp. Ther. 286:1020-1025(1998).
 RN [6]
 RP NUCLEOTIDE SEQUENCE [MRNA] (ISOFORM PSMA-1), AND CHARACTERIZATION.
 RC TISSUE-Prostate;
 RX MEDLINE-99185063; PubMed-10085079; DOI=10.1074/jbc.274.13.8470;
 RA Pangalos M.N., Neefs J.-M., Somers M., Verhasselt P., Bekkers M.,
 van der Helm L., Fraiponts E., Ashton D., Gordon R.D.;
 RT "Isolation and expression of novel human glutamate carboxypeptidases
 RT with N-acetylated alpha-linked acidic dipeptidase and dipeptidyl
 RT peptidase IV activity.";
 RL J. Biol. Chem. 274:8470-8483(1999).
 RN [7]
 RP NUCLEOTIDE SEQUENCE [MRNA] (ISOFORMS PSMA-1 AND PSMA-2), AND VARIANT
 RP TYR-475.
 RC TISSUE=Jejunum;
 RX PubMed-11092759; DOI=10.1093/hmg/9.19.2837;
 RA Devlin A.M., Ling E.-H., Pearson J.M., Fernando S., Clarke R.,
 Smith A.D., Halsted C.H.;
 RT "Glutamate carboxypeptidase II: a polymorphism associated with lower
 RT levels of serum folate and hyperhomocysteinemia.";
 RL Hum. Mol. Genet. 9:2837-2844(2000).
 RN [8]
 RP NUCLEOTIDE SEQUENCE [GENOMIC DNA] (ISOFORM PSMA-5).
 RA Peace D.J., Zhang Y., Holt G., Ferrer K.T., Heller M., Sosman J.A.,
 RA Xue B.H.;
 RT "Identification of three novel splice variants of prostate-specific
 RT membrane antigen.";
 RL Submitted (NOV-1998) to the EMBL/GenBank/DBJ databases.
 RN [9]
 RP NUCLEOTIDE SEQUENCE [MRNA], AND TISSUE SPECIFICITY.
 RC TISSUE=Liver;
 RX PubMed-14716746; DOI=10.1002/pros.10319;
 RA O'Keefe D.S., Bacich D.J., Heston W.D.W.;

RT "Comparative analysis of prostate-specific membrane antigen (PSMA)
 RL versus a prostate-specific membrane antigen-like gene.";
 RL Prostate 58:200-210(2004).
 RN [10]
 RP PARTIAL NUCLEOTIDE SEQUENCE [MRNA] (ISOFORMS PSMA-3 AND PSMA-4).
 RA Lupold S.E., Criley S.C., Coffey D.S.;
 RT "Alternative Splicing of the prostate-specific membrane antigen.";
 RL Submitted (APR-2000) to the EMBL/GenBank/DBJ databases.
 RN [11]
 RP PROTEIN SEQUENCE OF 60-74, AND SUBCELLULAR LOCATION.
 RC TISSUE=Prostatic carcinoma;
 RX MEDLINE=99025849; PubMed=9809977;
 RA Grauer L.S., Lawler K.D., Marignac J.L., Kumar A., Goel A.S.,
 RA Wolfert R.L.;
 RT "Identification, purification, and subcellular localization of
 RL prostate-specific membrane antigen PSM' protein in the LNCaP prostatic
 RT carcinoma cell line.";
 RL Cancer Res. 58:4787-4789(1998).
 RN [12]
 RP ALTERNATIVE SPLICING.
 RA Bzdega T., She D., Turi T., Wroblewska B., Neale J.H.;
 RT "Molecular cloning of alternatively spliced variants of the peptidase
 RL against N-acetylaspartylglutamate (NAAG) from human and rat nervous
 RT systems.";
 RL Abstr. - Soc. Neurosci. 24:579-579(1998).
 RN [13]
 RP CHARACTERIZATION.
 RX MEDLINE=98288196; PubMed=9622670; DOI=10.1016/S0006-8993(98)00244-3;
 RA Luthi-Carter R., Barczak A.K., Speno H.D., Coyle J.T.;
 RT "Hydrolysis of the neuropeptide N-acetylaspartylglutamate (NAAG) by
 RL cloned human glutamate carboxypeptidase II.";
 RL Brain Res. 795:341-348(1998).
 RN [14]
 RP DOMAIN STRUCTURE.
 RX MEDLINE=97330810; PubMed=9187245; DOI=10.1016/S0167-4838(97)00008-3;
 RA Rawlings N.D., Barrett A.J.;
 RT "Structure of membrane glutamate carboxypeptidase.";
 RL Biochim. Biophys. Acta 1339:247-252(1997).
 RN [15]
 RP MUTAGENESIS.
 RX MEDLINE=99102317; PubMed=9882712;
 RA Speno H.S., Luthi-Carter R., Macias W.L., Valentine S.L.,
 RA Joshi A.R.T., Coyle J.T.;
 RT "Site-directed mutagenesis of predicted active site residues in
 RL glutamate carboxypeptidase II.";
 RL Mol. Pharmacol. 55:179-185(1999).
 RN [16]
 RP GLYCOSYLATION AT ASN-76; ASN-336; ASN-459; ASN-476 AND ASN-638.
 RX MEDLINE=22660472; PubMed=12754519; DOI=10.1038/nbt827;
 RA Zhang H., Li X.-J., Martin D.B., Aebersold R.;
 RT "Identification and quantification of N-linked glycoproteins using
 RL hydrazide chemistry, stable isotope labeling and mass spectrometry.";
 RL Nat. Biotechnol. 21:660-666(2003).
 RN [17]
 RP GLYCOSYLATION AT ASN-51; ASN-76; ASN-121; ASN-140; ASN-153; ASN-195;
 RP ASN-336; ASN-459; ASN-476 AND ASN-638, AND MUTAGENESIS OF ASN-51;
 RP ASN-76; ASN-121; ASN-140; ASN-153; ASN-195; ASN-336; ASN-459; ASN-476;
 RP ASN-638 AND THR-640.
 RX PubMed=15152093; DOI=10.1110/ps.04622104;
 RA Barinka C., Sacha P., Sklenar J., Man P., Bezouska K., Slusher B.S.,
 RA Konvalinka J.;
 RT "Identification of the N-glycosylation sites on glutamate
 RL carboxypeptidase II necessary for proteolytic activity.";
 RL Protein Sci. 13:1627-1635(2004).
 CC -I- FUNCTION: Has both folate hydrolase and N-acetylated-alpha-linked-
 CC acidic dipeptidase (NAALADase) activity. Has a preference for tri-
 CC alpha-glutamate peptides. In the intestine, required for the
 CC uptake of folate. In the brain, modulates excitatory
 CC neurotransmission through the hydrolysis of the neuropeptide, N-
 CC acetylaspartylglutamate (NAAG), thereby releasing glutamate.
 CC Isoforms PSM-4 and PSM-5 would appear to be physiologically

CC irrelevant. Involved in prostate tumor progression.
 CC -!- FUNCTION: Also exhibits a dipeptidyl-peptidase IV type activity.
 CC In vitro, cleaves Gly-Pro-AMC.
 CC -!- CATALYTIC ACTIVITY: Release of an unsubstituted, C-terminal
 CC glutamyl residue, typically from Ac-Asp-Glu or folylpoly-gamma-
 CC glutamates.
 CC -!- COFACTOR: Binds 2 zinc ions per subunit. Required for NAALADase
 CC activity.
 CC -!- ENZYME REGULATION: The NAALADase activity is inhibited by beta-
 CC NAAG, quisqualic acid, 2-(phosphonomethyl) pentanedioic acid
 CC (PMPA) and EDTA. Activated by cobalt.
 CC -!- BIOPHYSICOCHEMICAL PROPERTIES:
 CC pH dependence:
 CC Stable at pH greater than 6.5;
 CC -!- SUBCELLULAR LOCATION: Cell membrane; Single-pass type II membrane
 CC protein. Isoform PSMA-1; Cytoplasm.
 CC -!- ALTERNATIVE PRODUCTS:
 CC Event-Alternative splicing; Named isoforms-6;
 CC Comment-Experimental confirmation may be lacking for some
 CC isoforms;
 CC Name=PSMA-1;
 CC IsoId=Q04609-1; Sequence=Displayed;
 CC Name=PSMA-2;
 CC IsoId=Q04609-2; Sequence=VSP_005341;
 CC Name=PSMA-3;
 CC IsoId=Q04609-3; Sequence=VSP_005342;
 CC Name=PSMA-4;
 CC IsoId=Q04609-4; Sequence=VSP_005339, VSP_005340;
 CC Name=PSMA-5;
 CC IsoId=Q04609-5; Sequence=VSP_005337, VSP_005338;
 CC Name=PSMA-6;
 CC IsoId=Q04609-6; Sequence=VSP_005336;
 CC -!- TISSUE SPECIFICITY: Highly expressed in prostate epithelium. Also
 CC expressed, in the small intestine, brain, kidney, liver, spleen,
 CC colon, trachea, spinal cord and the capillary endothelium of a
 CC variety of tumors. Expressed specifically in jejunum brush border

Query Match 100.0%; Score 3983; DB 1; Length 750;
 Best Local Similarity 100.0%; Pred. No. 1.6e-266;
 Matches 750; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy      1 MNLLHETDSAVATARRPRMLCAGALVLAGGFLLGLFLGFWFIKSSNEATNITPKHNMKA 60
Db      1 MNLLHETDSAVATARRPRMLCAGALVLAGGFLLGLFLGFWFIKSSNEATNITPKHNMKA 60

Qy      61 FLDELKAENIKKFLYNFTQIPHLAGTEQNQLAKQIQSQMKFEGLDSVELAHYDVLLSY 120
Db      61 FLDELKAENIKKFLYNFTQIPHLAGTEQNQLAKQIQSQMKFEGLDSVELAHYDVLLSY 120

Qy      121 NKTHPNYISIIINEGNEIFNTSLFEP PPPGYENVSDIVPPFSAFSPQGMPEGDLVYVNYA 180
Db      121 NKTHPNYISIIINEGNEIFNTSLFEP PPPGYENVSDIVPPFSAFSPQGMPEGDLVYVNYA 180

Qy      181 RTEDFFKLERDMKINCSGKVIARYGKVFGRGNKVNAQLAGAKGVILYS DPADYFAPGVK 240
Db      181 RTEDFFKLERDMKINCSGKVIARYGKVFGRGNKVNAQLAGAKGVILYS DPADYFAPGVK 240

Qy      241 SYPDGWNLPGGGVQRGNILNLNGAGDPLTPGYPANAYARRGIAEAVGLSPVHPIGYY 300
Db      241 SYPDGWNLPGGGVQRGNILNLNGAGDPLTPGYPANAYARRGIAEAVGLSPVHPIGYY 300

Qy      301 DAQKLLKMGSGAPPDSSWRGSLKVPYNVGPFTGNFSTQKVKMHISTNEVTRIYNVIG 360
Db      301 DAQKLLKMGSGAPPDSSWRGSLKVPYNVGPFTGNFSTQKVKMHISTNEVTRIYNVIG 360

Qy      361 TLRGAVEPDRYVILGHRDSWVEGGIDPQSGAAVVEIVRSFGTLKKEGWPRRTILFAS 420
Db      361 TLRGAVEPDRYVILGHRDSWVEGGIDPQSGAAVVEIVRSFGTLKKEGWPRRTILFAS 420

Qy      421 WDAEEFGLLGSTWAEENSRLQERGVAYINADSSIEGNYTLRVDCPTPLMYSLVHNLTK 480

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Db	481	LKSPDEGFEGKSLYESWTKKSPSPFSGMPRISKLGSGNDFEVFFQRLGIASGRARYTKN	540
Qy	541	WETNKFSGYPLYHSVYETIYELVEKFYDPMFKYHLTVAQVRGGMVFELANSIVLPFDCRDY	600
Db	541	WETNKFSGYPLYHSVYETIYELVEKFYDPMFKYHLTVAQVRGGMVFELANSIVLPFDCRDY	600
Qy	601	AVVLRKYADKIYISIMKHPQEMKTYSVSFDLSFSAVKNFTEIASKFSERLQDFDKSNPIV	660
Db	601	AVVLRKYADKIYISIMKHPQEMKTYSVSFDLSFSAVKNFTEIASKFSERLQDFDKSNPIV	660
Qy	661	LRMNDQLMFLERAFIDPLGLPDRPFYRHVIYAPSSHINKYAGESFPGLYDALFDIESKVD	720
Db	661	LRMNDQLMFLERAFIDPLGLPDRPFYRHVIYAPSSHINKYAGESFPGLYDALFDIESKVD	720
Qy	721	PSKAWGEVKRQIYVAAFTVQAAAETLSEVA	750
Db	721	PSKAWGEVKRQIYVAAFTVQAAAETLSEVA	750